

National Jewish Hospital at Denver

A FREE NON-SECTARIAN, TUBERCULOSIS MEDICAL CENTER
TREATMENT...RESEARCH...EDUCATION...REHABILITATION

DEPARTMENT OF
RESEARCH AND LABORATORIES

April 1, 1954

3800 EAST COLFAX AVE.
DENVER 6, COLORADO

Dr. Joshua Lederberg
Department of Genetics
College of Agriculture
University of Wisconsin
Madison, Wisconsin

Dear Doctor Lederberg:

It was a very pleasant surprise to receive from you your recent publications. As you may remember, I had the pleasure of listening to one of your seminars before van Niel's group at Pacific Grove in the summer of 1950. Since then I have received some news of your activities through Bernie Davis and Ted Puck.

I want to take this opportunity to extend to you the hospitality of the Department of Research and Laboratories of the National Jewish Hospital. I do this not only because of your reputation as a highly intelligent person, in general, but also because we have become involved in problems of microbial genetics and physiology through the back door, as it were. Please find enclosed a reprint which serves as the basis of our present activities. You will note that the paper was submitted for publication nearly a year ago. Since that time we have become involved not only in problems of microbial nutrition and metabolism relating to "mutation" to isoniazid resistance, but also in host physiology as it relates to susceptibility to infection with tubercle bacilli. In particular, we have accumulated evidence, not yet submitted for publication, that certain isoniazid-resistant mutants of tubercle bacilli are highly attenuated for "normal" guinea pigs because of their inability to manifest catalase activity; and in some preliminary experiments we have observed a marked reduction in the catalase activity of the mononuclear phagocytes of tuberculous guinea pigs (guinea pigs hypersensitive to tuberculin, compared with "normal" guinea pigs).

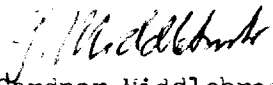
Dr. Bernard Schaefer in this department has been engaged in studying the growth requirements of catalase-positive and catalase-negative isoniazid-resistant mutants of tubercle bacilli, and only yesterday decided to embark upon attempts to apply your replica plating techniques in efforts to simplify such studies. As you probably know, the notoriously hydrophobic properties of tubercle bacilli constitute an obstacle which has prevented us from attempting this type of investigation before now. However, perhaps with the use of Tween 80 incorporated in the agar medium we shall be able to overcome this obstacle.

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Thus far we have been able, by other methods, to identify at least 4 different types of isoniazid-resistant mutants differentiable by their growth requirements and catalase activities. These organisms grow so slowly that any method which might decrease the number of plates required would be most welcome in further studies. Incidentally, rapidly multiplying saprophytic mycobacteria cannot be used in such investigations--not even for orientation purposes: this we have established, to our great dismay.

If, by any chance, you find it possible to come to Colorado this summer, with or without your family, we would appreciate it very much if you would stop in Denver to see us and give us any advice which your experience and understanding will certainly suggest. In point of fact, the above paragraphs are specifically designed to tease you into coming.

Cordially yours,


Gardner Middlebrook, M.D.
Director
Research and Laboratories

GM:mwp
Encl.